MAR 3 0 2012

510(k) Summary Report

BioPlex® 2200 Anti-Phospholipid Syndrome (APLS) IgG and IgA kits

510(k) Number: k103834 Date Prepared: March 28, 2012

Bio-Rad Laboratories hereby submits this Special 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex® 2200 APLS IgG and IgA.

1. Applicant/Sponsor

Submitter	Contact Person
Bio-Rad Laboratories, Inc BioPlex Division 5500 E. Second Street Benicia, CA 94510	Juang Wang Regulatory Affairs Representative Phone: (510)741-4609 Fax: (510)741-3941

2. Device Name

Proprietary Name: BioPlex® 2200 APLS IgG Kit
BioPlex® 2200 APLS IgG Calibrator Set
BioPlex® 2200 APLS IgG Control Set
BioPlex® 2200 APLS IgA Kit
BioPlex® 2200 APLS IgA Calibrator Set
BioPlex® 2200 APLS IgA Control Set

Common/Usual Name: Multi-Analyte Detection System: APLS IgG and IgA IgG

Classification Name:

system, test, anticardiolipin immunological system
test,antibodies,b2 - glycoprotein I (b2 - gpi)
calibrator, multi-analyte mixture
single-analyte controls, all kinds (assayed and unassayed)

3. Regulatory Information

Product Code	Classification	Regulation Section	Panel
system, test, anticardiolipin immunological (MID)	Class II	21 CFR § 866.5660, Multiple autoantibodies immunological test system.	Immunology
system,test,antibodies,b2 - glycoprotein I (b2 - gpi) (MSV)	Class II	21 CFR § 866.5660, Multiple autoantibodies immunological test system.	Immunology
Calibrator, multi-analyte mixture (JIX)	Class II	21 CFR § 862.1150 – Calibrator	Clinical Chemistry
single (specified) analyte controls (assayed and unassayed) (JJX)	Class I	21 CFR § 862.1660 – Quality control Material (Assayed and Unassayed)	Clinical Chemistry

4. Predicate Devices

K022992 REAADS anti-Cardiolipin IgG/IgM Semi-Quantitative Test Kit (2 assays)
K022990 REAADS IgA anti-Cardiolipin Semi-Quantitative Test Kit
K013080 REAADS anti-Beta 2 Glycoprotein I IgG Test Kit
K013079 REAADS anti-Beta 2 Glycoprotein I IgA Test Kit

5. Device Description

The BioPlex® 2200 APLS IgG and IgA IgG kit uses multiplex flow immunoassay, a methodology that greatly resembles traditional EIA, but permits simultaneous detection and identification of many antibodies in a single tube. "APLS" is an acronym for Anti-Phospholipid Syndrome.

Two (2) different populations of dyed beads are coated with the antigens associated with Cardiolipin (CL) and Beta-2-Glycoprpotein I (ß2GPI), respectively. The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, anti-human IgG or IgA antibody, conjugated to phycoerythrin (PE) is added to the dyed beads and this mixture is incubated at 37°C. The excess conjugate is removed in another wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of analyte captured is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity (RFI).

Three additional dyed beads, an Internal Standard Bead (ISB), a Serum Verification Bead (SVB) and a Reagent Blank Bead (RBB) are present in each reaction mixture to normalize detector response, to verify the addition of serum to the reaction vessel and the absence of significant non-specific binding in serum or plasma. Refer to the BioPlex 2200 System Operation Manual for more information.

The instrument is calibrated using a set of seven (7) distinct calibrator vials for APLS IgG kit and a set of three (3) distinct calibrator vials for the APLS IgA kit, all supplied separately by Bio-Rad Laboratories. For each aCL IgG and aß2GPI IgG, four (4) vials representing four (4) different antibody concentrations are used for semi-quantitative calibration. For each aCL IgA and aß2GPI IgA assay, two (2) vials representing two (2) different antibody concentrations are used for semi-quantitative calibration. The cut-off value and assignment of the calibrators are determined by performing concordance testing and Receiver Operator Characteristic (ROC) analysis, using clinical diagnosis as the standard. The results for aCL IgG and aCL IgA are expressed in GPL-U/mL and APL-U/mL units, respectively. The results for aß2GPI IgG and aß2GPI IgA are each expressed in U/mL units.

The APLS IgG and APLS IgA Control Sets are intended for use as an assayed quality control to monitor the overall performance of the BioPlex® 2200 instrument and BioPlex 2200 APLS IgG and IgA reagent packs in the clinical laboratory.

Each of the APLS IgG and APLS IgA Control Sets includes a negative control and a positive control for each aCL IgG or IgA and aß2GPI IgG or IgA in a human serum matrix made from defibrinated plasma, containing antibodies present for analytes within the APLS IgG or IgA kit. The positive controls are manufactured to give positive results, with values above the cutoff for each specific bead. The negative control is manufactured to give negative results, with values below the cutoff for each specific bead. The negative control must have a negative result, and the positive control must have a positive result.

6. BioPlex® 2200 APLS IgG and IgA Kit Components

The BioPlex 2200® APLS IgG(665-1950) and IgA (665-2150) kit contains supplies sufficient for 100 tests.

Vial	Description
Bead Set	One (1) 10 mL vial, containing dyed beads coated with CL and ß2GPI; an Internal Standard bead (ISB), a Serum Verification bead (SVB), and a Reagent Blank bead (RBB) in a MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with glycerol and protein stabilizers (porcine). ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
Conjugate	One (1) 5 mL vial, containing phycoerythrin conjugated murine monoclonal anti-human IgG or

	IgA antibody and phycoerythrin conjugated murine monoclonal anti-human FXIII antibody in MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with protein stabilizers (bovine). ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
Sample Diluent	One (1) 10 mL vial, containing buffer with protein stabilizers (bovine and murine). ProClin 300 (0.3%), sodium benzoate (≤0.1%) and sodium azide (< 0.1%) as preservatives.

Additional Required Items, Available from Bio-Rad:

Catalog #	Description
663-1900	BioPlex 2200 APLS IgG Calibrator Set: Seven 0.5 mL vials, each containing human antibodies to CL and/or ß2GPI, in a human serum matrix made from defibrinated plasma. All calibrators contain ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
663-2100	BioPlex 2200 APLS IgA Calibrator Set: Three 0.5 mL vials, each containing human antibodies to CL and/or ß2GPI, in a human serum matrix made from defibrinated plasma. All calibrators contain ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
663-1930	BioPlex 2200 APLS IgG Control Set: Four 1.5 mL Positive Control serum vials, each containing human antibodies to CL or ß2GPI, in a human serum matrix made from defibrinated plasma; and two Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All controls contain ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
663-2130	BioPlex 2200 APLS IgA Control Set: Four 1.5 mL Positive Control serum vials, each containing human antibodies to CL or ß2GPI, in a human serum matrix made from defibrinated plasma; and two Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All controls contain ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
660-0817	BioPlex 2200 Sheath Fluid: Two 4 L bottles containing Phosphate Buffered Saline (PBS). ProClin® 300 (0.03%) and sodium azide (<0.1%) as preservatives.
660-0818	BioPlex 2200 Wash Solution: One 10 L bottle

Catalog #	Description
	containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin® 300 (≤0.03%) and sodium azide (<0.1%) as preservatives.
660-0000	BioPlex 2200 Instrument and Software System.

7. Intended Use

BioPlex® 2200 APLS IgG and IgA Kits

The BioPlex® 2200 APLS IgG and IgA kits are multiplex flow immunoassays intended for the semi-quantitative detection of IgG and IgA antibodies to Cardiolipin (CL) and Beta-2 Glycoprotein I (ß2GPI) in human serum and plasma (lithium heparin, sodium heparin, and sodium citrate). In conjunction with other clinical findings, the test systems are used as an aid in the diagnosis of primary Antiphospholipid Syndrome (APS) and those secondary to systemic lupus erythematosus (SLE) or SLE-like disorders.

The BioPlex 2200 APLS IgG and IgA kits are intended for use with the Bio-Rad BioPlex 2200 System

BioPlex® 2200 APLS IgG and IgA Calibrator Sets

The BioPlex® 2200 APLS IgG and IgA Calibrator Sets are intended for the calibration of the corresponding BioPlex® 2200 APLS IgG and IgA Reagent Packs.

BioPlex® 2200 APLS IgG and IgA Control Sets

The BioPlex® 2200 APLS IgG and IgA Control Sets are intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 instrument and the corresponding BioPlex 2200 APLS IgG and IgA Reagent Packs in the clinical laboratory. The performance of the BioPlex 2200 APLS IgG and IgA Control Sets has not been established with any other anti-Cardiolipin and anti- Beta-2 Glycoprotein I IgG or IgA APS assays.

8. Technological Characteristics and Substantial Equivalence

The following tables summarize the similarities and differences between the BioPlex 2200 APLS IgG and IgA kit and the predicate devices used in comparative studies with the BioPlex® 2200 APLS IgG and IgA kits.

BioPlex 2200® APLS IgG and IgA Kits vs. Predicate Devices - Similarities

Similarities between Components / Materials	BioPlex® 2200 APLS IgG and IgA Kits	READS Anti-Cardiolipin IgG and IgA Semi-Quantitative Test Kits (K022992 IgG, K022990 IgA)	READS Anti--β2 Glycoprotein I IgG and IgA Semi-Quantitative Test Kits (K013080, K013077, K013079)
Intended Use	The BioPlex® 2200 APLS IgG and IgA kits are multiplex flow immunoassays intended for the semi-quantitative detection of IgG and IgA antibodies to Cardiolipin (CL) and Beta-2 Glycoprotein I (ß2GPI) in human serum and plasma (lithium heparin, sodium heparin, and sodium citrate). In conjunction with other clinical findings, the test systems are used as an aid in the diagnosis of primary Antiphospholipid Syndrome (APS) and those secondary to systemic lupus erythematosus (SLE) or SLE-like disorders. The BioPlex 2200 APLS IgG and IgA kits are intended for use with the Bio-Rad BioPlex 2200 System.	An enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative determination of anti-cardiolipin IgG, and IgA antibodies in human serum or plasma in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (anti-phospholipid syndrome)	An enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative determination of anti-β2 Glycoprotein I (β_2GPI) IgG and IgA antibodies in human serum or citrated plasma in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (anti-phospholipid syndrome)
Capture Antigen	Cardiolipin and β2 Glycoprotein I	Same	Same
Assay Type	Semi-Quantitative detection	Same	Same
Analyte Detected	Human IgG or IgA antibodies to Cardiolipin and β2 Glycoprotein I	Same	Same
Specimen Type	Serum and plasma	Same	Same

Similarities between Components / Materials	BioPlex® 2200 APLS IgG and IgA Kits	READS Anti-Cardiolipin IgG and IgA Semi-Quantitative Test Kits (K022992 IgG, K022990 IgA)	READS Anti--β2 Glycoprotein I IgG and IgA Semi-Quantitative Test Kits (K013080, K013077, K013079)
Controls	Negative and Positive Controls	Same	Same
Calibrator(s)	Multiple Calibrators	Same	Same

BioPlex 2200® APLS IgG and IgA Kits vs. Predicate Device - Differences

Differences between Components / Materials	BioPlex® 2200 APLS IgG and IgA Kits	READS Anti-Cardiolipin IgG and IgA Semi-Quantitative Test Kits (K022992 IgG, K022990 IgA)	READS Anti--β2 Glycoprotein I IgG and IgA Semi-Quantitative Test Kits (K013080, K013077, K013079)
Assay Technology	Automated Multiplex flow immunoassay	Manual, microtitre plate format, Enzyme-linked Immunosorbent assay (ELISA)	Manual, microtitre plate format, Enzyme-linked Immunosorbent assay (ELISA)
Conjugate Antibody	Phycoerythrin conjugated murine monoclonal anti-human IgG or IgA.	Goat anti-human IgG, or IgA HRP-conjugated antibody solution	Goat anti-human IgG or IgA HRP-conjugated antibody solution
Substrate	None	Tetramethlybenzidine (TMB) and hydrogen peroxide (H_2O_2)	Tetramethlybenzidine (TMB) and hydrogen peroxide (H_2O_2)
Specimen Type	Serum and plasma (citrated and heparin)	Serum and plasma (except heparin)	Serum and plasma (citrated)
Signal Detection	Fluorescence	Color, read at 450nm	Color, read at 450nm
Solid Phase	Antigen-coated paramagnetic microbead reagent. Microbeads are infused with red and infrared fluorescent dyes for bead classification. Green fluorescence from the immunoassay label is used for analyte measurement.	Antigen-coated solid phase microtitre wells	Antigen-coated solid phase microtitre wells

Differences between Components / Materials	BioPlex® 2200 APLS IgG and IgA Kits	REAADS Anti-Cardiolipin IgG and IgA Semi-Quantitative Test Kits (K022992 IgG, K022990 IgA)	REAADS Anti--β2 Glycoprotein I IgG and IgA Semi-Quantitative Test Kits (K013080, K013077, K013079)
Calibrator(s)	4 levels of Calibrator for IgG 2 levels of Calibrator for IgA	3 levels of Calibrator for IgG and IgA	3 levels of Calibrator for IgG and IgA
Calibrator Range	Anti-Cardiolipin : IgG :1.6 – 112 GPL U/mL IgA : 0.5 – 28 APL U/mL Anti-Beta-2 Glycoprotein I : IgG : 1.4 – 112 U/mL IgA : 0.6 – 28 U/mL	Anti-Cardiolipin : IgG :0 - 100 GPL- U/mL IgA : 0 – 80 APL U/mL	Anti-Beta-2 Glycoprotein I : IgG : 0 - 200 U//mL IgA : 0- 200 U/mL
Calibrators and Controls	Sold separately	Kit components	Kit components
Quantitation	Results are determined from a standard calibration curve utilizing a point-to-point calculation.	Results are derived from a linear regression analysis	Results are derived from a linear regression analysis

9. Performance Characteristics

A. Analytical Performance

i. Precision/Reproducibility

EP15-A2 reproducibility studies were conducted to evaluate the reproducibility of the BioPlex 2200 APLS IgG and IgA kits on the BioPlex 2200 instrument. Reproducibility studies were based on the principles described in Clinical and Laboratory Standards Institute (CLSI) EP15-A2, *User Verification of Performance for Precision and Trueness.*

The study was performed at one clinical trial site. One lot each of BioPlex 200 APLS IgG and IgA reagent packs, Calibrator Sets and Control Sets was evaluated. Four panels were made from serum and plasma (lithium heparin, sodium heparin and sodium citrate) plus controls. Each panel of 8 samples covering the assay measuring range was tested in quadruplicate over five days (4 replicates x 1 run x 5 days x 1 testing site = 20 replicates per panel member) according to CLSI EP15-A2 guideline.

The data were analyzed for within-run, between-day, and total precision and the standard deviation (SD) and percent coefficient of variation (%CV) were calculated.

The within-run precision and total precision in %CV for positive samples near the cut-off for anti-Cardiolipin IgG and IgA (20 GPL-U/mL, MPL-U/mL, and APL-U/mL) and for anti-Beta-2 Glycoprotein I IgG and IgA (20 U/mL) in all sample matrices are shown below.

BioPlex 2200 APLS Assay	Within run (%CV)		Total (%CV)	
	Min	Max	Min	Max
aCL IgG	1.4	8.9	2.3	9.2
aß2GPI IgG	1.3	6.2	1.7	7.0
aCL IgA	2.2	4.3	2.5	4.3
aß2GPI IgA	2.0	4.2	2.0	4.5

ii. Linearity/Assay Reportable Ranges

Three (3) APLS anti-Cardiolipin and anti-β_2GPI IgG and IgA positive patient samples were tested to demonstrate linearity. These samples were diluted with immunodepleted serum according to CLSI EP06-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach.*

Each sample and dilution was evaluated in replicates of four using one APLS IgG and IgA IgG lot on one instrument. Linear and polynomial regression analysis of APLS IgG and IgA IgG recovery *vs.* sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

The regression parameters (slope, intercept and r^2) of the observed values vs. predicted values are show below. The BioPlex 2200 APLS IgG and IgA IgG assay demonstrated linearity from 0 to 112 GPL-U/mL for aCL IgG and, 0 to 28 APL-U/mL for aCL IgA and 0 to 112 U/mL for.aβ_2GPI IgG and 0 to 28 U/mL for aβ_2GPI IgA.

APLS Assays	Sample ID	Conc.	Slope	Intercept	r^2
aCL IgG (GPL-U/mL)	APS0471A	50.8	0.9998	0.0056	0.9999
	APS0882	56.1	1.0001	0.0105	0.9994
	APS0893	43.3	1.0009	-0.0182	0.9964
	APS0471B	104.5	1.0004	-0.0033	0.9991
	APS0486	89.3	1.0008	-0.0307	0.9982
	791227A4	92.7	1.0003	-0.0112	0.9999
aB2GPI IgG (U/mL)	APS0882	56.8	0.9996	0.0104	0.9999
	APS0893	45.3	0.9995	0.0104	0.9978
	791250G	54.9	1.0000	0.0010	0.9758
	APS0471	95.1	1.0003	-0.0113	0.9991
	APS0486	98.4	1.0001	-0.0038	0.9958
	791227G4	100.4	1.0008	-0.0049	0.9997
aCL IgA (APL-U/mL)	APS0485	26.4	0.9999	0.0012	0.9932
	APS0885	27.1	1.0014	0.0102	0.9958
	APS0891	30.2	1.0011	-0.0169	0.9836
aB2GPI IgA (U/mL)	APS0485	33.2	1.0001	0.0009	0.9900
	APS0885	33.9	1.0022	-0.0356	0.9937
	APS0891	28.1	1.0017	-0.0251	0.9758

The BioPlex 2200 system does not support an on-board dilution feature for testing over-range samples.

iii. Traceability of Calibrators/Controls

There is no international or certified reference material available for APLS aCL and aβ_2GPI IgG and IgA assays.

The BioPlex 2200 APLS IgG or IgA Calibrator Set is intended for the calibration of the BioPlex 2200 APLS IgG or IgA Reagent Pack, respectively.

The BioPlex 2200 APLS IgG or IgA Reagent Kit is calibrated using a set of four distinct serum based calibrators for IgG ; a set of two distinct serum based calibrators for IgA, which are used to establish points of reference for determining the presence of IgG or IgA in human specimens. The calibrators are made in human serum matrix derived from defibrinated plasma depleted of IgG plus known concentrations of anti-Beta-2Glycoprotein I (aB2GPI) IgG or IgA or anti-Cardiolipin (aCL) IgG or IgA derived from defibrinated human plasma. The Calibrators are manufactured independently from the controls, and are stabilized with ≤0.3% ProClin® 300, ≤0.1% sodium benzoate, and ≤0.1% sodium azide.

Calibrator assignment is established for matched lots of BioPlex 2200 APLS IgG or IgA kit and calibrators using a master set of calibrators as reference and replicate analyses on multiple BioPlex 2200 instruments.

For the aCL IgG, and aCL IgA assays, the assays are calibrated in units of GPL-U/mL and APL-U/mL, respectively. For aß2GPI IgG ,and aß2GPI IgA, the assays are calibrated in units of U/mL.

The BioPlex 2200 APLS IgG or IgA Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 APLS IgG or IgA Kit in the clinical laboratory, respectively. The performance of the BioPlex 2200 APLS IgG or IgA Control Set has not been established with any other Antiphospholipid assay.

The controls are provided in liquid form in a human serum matrix made from defibrinated plasma stabilized with ≤0.3% ProClin® 300, 0.1% sodium benzoate and ≤0.1% sodium azide. The positive control contains known concentrations of anti-Beta-2 Glycoprotein I (aB2GPI) IgG or IgA and anti-Cardiolipin (aCL) IgG or IgA derived from human plasma.

The negative control is provided as a human serum matrix made from defibrinated plasma that has been tested to give results with values below the cut-off for each assay. The positive control is prepared by blending human disease state serum with negative serum matrix and is manufactured to give results with values above the assay cut-off. The blending formulation for a specific lot of positive control is derived by a theoretical calculation. Based on this calculation, a pilot blend is prepared and tested. The results are used to adjust the spike volumes until an optimized manufacturing formulation that meets the target control values is achieved.

iv. Limit of Detection

The Limit of Detection (LoD) of BioPlex 2200 APLS IgG and IgA was determined by assaying low negative and blank samples in replicates of

fifty (50). The LoD was calculated according to CLSI EP17-A, *Protocols for Determination of Limits of Detection and Limits of Quantitation.* The calculated LoD for the APLS IgG and IgA assay is listed below..

BioPlex 2200 APLS Assay	LoD
aCL IgG	1.6 GPL-U/mL
aß2GPI IgG	1.4 U/mL
aCL IgA	0.5 APL-U/mL
aß2GPI IgA	0.6 U/mL

v. Analytical Specificity

Interfering Substances

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex 2200 APLS IgG and IgA assay.

Samples were prepared by blending a pool of negative human serum with samples positive for anti-Cardiolipin (aCL) IgG or IgA and anti-Beta-2Glycoprotein I ($a\beta_2GPI$) IgG or IgA to achieve approximate values of 10, 20, 60 and 100 GPL for aCL IgG and 10, 20, 60 , 100 U/mL for $a\beta_2GPI$ IgG and 10, 20 APL-U/mL and U/mL for aCL and $a\beta_2GPI$ IgA with interferent or blank.

The study was conducted based on the principles described in Clinical and Laboratory Standards Institute (CLSI) EP7-A2, *Interference Testing in Clinical Chemistry*. No interference was observed with any of the substances tested. The substances and the maximum levels tested are shown in the table below.

Interfering Substances

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin, Unconjugated	≤ 20 mg/dL
Bilirubin, Conjugated	≤ 30 mg/dL
Cholesterol	≤ 500 mg/dL
Red Blood Cells	≤ 0.4% (v/v)
Gamma Globulin	≤ 6 g/dL
Triglycerides	≤ 3300 mg/dL
Protein (total)	≤ 12 g/dL
Beta-Carotene	≤ 0.6 mg/dL
Ascorbic Acid	≤ 3 mg/dL
Lithium Heparin	≤ 8000 units/dL
Sodium Heparin	≤ 8000 units/dL
Sodium Citrate	≤ 1000 mg/dL
EDTA	≤ 800 mg/dL

Cross-Reactivity

A cross-reactivity study was performed to determine if samples from individuals with various disease states and other potentially interfering factors interfere with test results from the BioPlex 2200 APLS IgG or IgA kit. Samples from individual with known disease states for potential cross reactivity listed in the table below were evaluated with the BioPlex 2200 APLS IgG, or IgA kit.

Table below shows the number (N) of samples containing potential cross reactants as disease state evaluated by the BioPlex APLS IgG and IgA. The cross reactivity was obtained as the positivity rate from the ratio of the number of samples scored positive by the BioPlex APLS IgG or IgA assays to the total number of cross reactant samples evaluated.

No significant cross reactivity for these potential cross reactants was observed.

Cross Reactivity - APLS IgG and IgA

Cross Reactant Disease State	N	aCL IgG		aB2GPI IgG		aCL IgA		aB2GPI IgA	
		# Pos	Positivity Rate	# Pos	Positivity Rate	# Pos	Positivity Rate	# Pos	Positivity Rate
Systemic Lupus Erythematosus	34	2	5.9%	2	5.9%	2	5.9%	2	5.9%
Scleroderma	20	0	0.0%	0	0.0%	1	5.0%	2	10.0%
Sjogrens	22	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Crohn's Disease	21	1	4.8%	0	0.0%	1	4.8%	1	4.8%
Ulcerative Colitis	20	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Rheumatoid Arthritis	12	0	0.0%	0	0.0%	1	8.3%	0	0.0%
Syphilis	15	1	6.7%	1	6.7%	0	0.0%	0	0.0%

vi. Assay Cut-off

The cutoff value and assignment of the calibrators are determined by performing concordance testing and Receiver Operator Characteristic (ROC) analysis. The study to determine the APLS IgG or IgA assay cutoff is comprised of two sample groups – one clinical cohort has 103 samples from patients diagnosed as primary and secondary APS and 208 from normal healthy and 123 from non-APS cardiac donors.

A cutoff of 20.0 GPL- or APL-U/mL for aCL IgG or IgA and 20 U/mL for $a\beta_2$GPI IgG, or IgA was established by optimizing for clinical accuracy.

The second cohort was comprised of the 208 samples from normal healthy donors plus 250 samples that were purchased based on vendor testing by aCL or $a\beta_2$GPI IgG and IgA assay. This cohort was used for determining predicate agreement using the cutoff established by clinical accuracy.

B. Comparative Performance

i. Comparative Testing

Method Comparison

Performance of the BioPlex 2200 APLS IgG, and IgA kits was evaluated against predicate device immunoassay.

The performance of the BioPlex 2200 APLS IgG and IgA kits was evaluated using a total of 804 specimens: 300 apparently healthy blood donors, 302 patients previously diagnosed with primary or secondary APS and 202 patients with other rheumatic or non-APS diseases that were tested at one clinical site. Patient specimens were purchased from commercial suppliers or rheumatology clinic labs and were frozen serum. Each sample was unique and was unlinked to patient identity and not individually identifiable. The study was evaluated for the clinical samples within the measuring range. The comparison results are presented in the tables below.

Healthy, Diagnosed APS and Non-APS			Predicate Immunoassay				
			Positive	Negative	Total	Positive % Agreement (95% CI)	Negative % Agreement (95%CI)
BioPlex APLS IgG	aCL IgG	Positive	99	14	113	75.6% (99/131) (67.6 - 82.1%)	88.9% (112/126) (82.2% - 93.3%)
		Negative	32	112	144		
		Total	131	126	257		
	$a\beta_2$GPI IgG	Positive	109	7	116	89.3% (109/122) (82.6 – 93.7%)	94.9% (130/137) (89.8 - 97.5%)
		Negative	13	130	143		
		Total	122	137	259		

Healthy, Diagnosed APS and Non-APS N=804			Predicate Immunoassay				
			Positive	Negative	Total	Positive % Agreement (95% CI)	Negative % Agreement (95%CI)
BioPlex APLS IgA	aCL IgA	Positive	39	24	63	88.6% (39/44) (76.0 – 95.0%%)	94.5% (416/440) (92.0 – 96.3%)
		Negative	5	416	421		
		Total	44	440	484		
	aβ2GPI IgA	Positive	57	1	58	40.1% (57/142) (32.4 – 48.4%)	99.6% (271/272) (97.9 - 99.9%)
		Negative	85	271	356		
		Total	142	272	414		

Matrix Comparison

Testing for matrix effects was conducted in accordance with CLSI EP9-A2 (Vol. 22, No. 19). More than 30 matched sets of serum and sodium citrate, lithium heparin, and sodium heparin plasma samples drawn from the same donor were acquired from a commercial source. The samples were spiked with aCL IgG or IgA and aB2GPI IgG or IgA positive sera as necessary in order to assemble a panel of samples to cover the measuring range of the assay. All samples were evaluated in replicates of two. Plasma values were compared to matched serum values. The regression correlation parameters for the slopes, intercepts and correlation coefficient (r) are shown below.

Matrix Comparison	N	BioPlex APLS Assay	Slope (95% CI)	Intercept (95% CI)	Correlation (r)
Lithium Heparin vs. Serum	32	aCL IgG	0.9720 (0.9457, 0.9984)	0.3788 (-1.0552, 1.8128)	0.9974
	32	$a\beta_2$GPI IgG	0.9756 (0.9488, 1.0023)	0.4377 (-1.1789, 2.0543)	0.9973
	36	aCL IgA	0.9767 (0.9090, 1.0445)	0.6309 (-0.3103, 1.5721)	0.9808
	36	$a\beta_2$GPI IgA	0.9865 (0.9249, 1.0480)	0.4698 (-0.2643, 1.2039)	0.9844
Sodium Heparin vs. Serum	32	aCL IgG	0.9885 (0.9531, 1.0239)	0.1921 (-1.7335, 2.1177)	0.9954
	32	$a\beta_2$GPI IgG	0.9889 (0.9555, 1.0222)	0.3559 (-1.6615, 2.3732)	0.9959
	36	aCL IgA	1.0244 (0.9641, 1.0847)	0.0753 (-0.7627, 0.9134)	0.9860
	36	$a\beta_2$GPI IgA	1.0150 (0.9520, 1.0779)	0.1714 (-0.5799, 0.9228)	0.9845
Sodium Citrate vs. Serum	32	aCL IgG	0.9398 (0.8757, 1.0039)	0.8087 (-2.6816, 4.2990)	0.9837
	32	$a\beta_2$GPI IgG	0.9351 (0.8730, 0.9972)	1.1299 (-2.6264, 4.8862)	0.9845
	36	aCL IgA	1.0096 (0.9480, 1.0713)	0.1181 (-0.7384, 0.9746)	0.9850
	36	$a\beta_2$GPI IgA	1.0061 (0.9500, 1.0622)	0.1801 (-0.4895, 0.8497)	0.9874

ii. Clinical Sensitivity and Specificity

The clinical studies involved testing 504 specimens including 302 diagnosed primary or secondary APS patients and 202 non-APS disease control patients. The BioPlex 2200 APLS IgG and IgA Sensitivity and Specificity are shown below.

Clinical Sensitivity and Specificity	BioPlex APLS IgG									
	aCL IgG					aβ2GPI IgG				
	Pos	Neg	Total	Sensitivity (95% CI)	Specificity (95% CI)	Pos	Neg	Total	Sensitivity (95% CI)	Specificity (95% CI)
Diagnosed APS Patients	188	98	286	65.7% (188/286)	98.5% (198/201)	186	100	286	65.0% (186/286)	99.0% (199/201)
Non-APS Disease Control	3	198	201	60.1 – 71.0%	95.7 – 99.5%	2	199	201	59.3 – 70.3%	96.4 – 99.7%
Total	191	296	487*			188	299	487*		

*17 samples exhibiting repeated instrument errors were excluded from the data analysis.

Clinical Sensitivity and Specificity	BioPlex APLS IgA									
	aCL IgA					aβ2GPI IgA				
	Pos	Neg	Total	Sensitivity (95% CI)	Specificity (95% CI)	Pos	Neg	Total	Sensitivity (95% CI)	Specificity (95% CI)
Diagnosed APS Patients	167	135	302	55.3% (167/302)	96.5% (195/202)	157	145	302	52.0% (157/302)	97.0% (196/202)
Non-APS Disease Control	7	195	202	49.7 – 60.8%	93.0 – 98.3%	6	196	202	46.4 – 57.6%	93.7 – 98.6%
Total	174	330	504			163	341	504		

The results of the BioPlex APLS IgG and IgA in each of disease category are shown below.

Disease Category	Number Enrolled	aCL IgG	aβ2GPI IgG	aCL IgA	aβ2GPI IgA
Primary APS (PAPS)	207*	119 (61%)	119 (61%)	108 (52%)	104 (50%)
Secondary APS (SAPS)	95*	67 (74%)	67 (74%)	59 (62%)	53 (56%)
Apparently Healthy Subjects	300	0 (0%)	0 (0%)	2 (1%)	2 (1%)
Systemic Lupus Erythrematosus	34	2 (6%)	2 (6%)	2 (6%)	2 (6%)
CREST	3	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Crohn's Disease	21	1 (5%)	0 (0%)	1 (5%)	1 (5%)
Fibromyalgia	20	0 (0%)	0 (0%)	1 (5%)	0 (0%)
Gout	14	0 (0%)	0 (0%)	1 (7%)	1 (7%)
Inflammatory Arthritis	4	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Osteoarthritis	12	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Scleroderma	20	0 (0%)	0 (0%)	1 (5%)	2 (10%)
Sjogrens	22	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ulcerative Colitis	20	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Wegeners Granulomatosis	5	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rheumatoid Arthritis	12	0 (0%)	0 (0%)	1 (8%)	0 (0%)
Syphilis	15*	0 (0%)	0 (0%)	0 (0%)	0 (0%)

* 195 PAPS, 91 SAPS and 14 Syphilis patient sample results were included in the data analysis for APLS IgG.

iii. Expected Values

Expected Values/Reference Range:

300 samples from apparently healthy donors including 132 males ranging in age from 7 to 85 and 168 females ranging in age from 14 to 83 were tested with BioPlex 2200 APLS IgG and IgA kits. The number of positive, mean value and 99th percentile of the BioPlex APLS IgG and IgA results are shown below. Results of <20.0 GPL- or APL-U/mL for aCL IgG or IgA and < 20.0 U/mL for aβ_2GPI IgG, or IgA are reported as negative and results ≥ 20.0

GPL- or APL-U/mL for aCL IgG or IgA and ≥ 20.0 U/mL for $a\beta_2$GPI IgG or IgA are reported as positive.

APLS Assay	N (%Positive)	Mean	99th percentile
aCL IgG	0 (0.0%)	<1.6 GPL –U/mL	8.5 GPL-U/mL
$a\beta_2$GPI IgG	0 (0.0%)	<1.4 U/mL	6.0 U/mL
aCL IgA	2 (0.7%)	1.4 APL- U/mL	14.5 APL-U/mL
$a\beta_2$GPI IgA	2 (0.7%)	1.3 U/mL	12.1 U/mL

Note: Each laboratory should establish its own reference range pertinent to their specific patient populations.

Prevalence:

The observed prevalence for the APLS IgG and IgA assay was determined using samples collected from apparently healthy blood donors (N=300) including 132 males ranging in age from 7 to 85 and 168 females ranging in age from 14 to 83 The results by gender and age are presented in the tables below.

Note: Each laboratory should establish frequency distributions for their specific patient populations.

Samples from Apparently Healthy Blood Donors
BioPlex2200 APLS IgG Prevalence Results by Age and Gender

Age	Gender	aCL IgG		$a\beta_2$GPI IgG	
		Pos/Total	% Prevalence	Pos/Total	% Prevalence
≤20	F	0/14	0.0%	0/14	0.0%
	M	0/5	0.0%	0/5	0.0%
21-30	F	0/13	0.0%	0/13	0.0%
	M	0/23	0.0%	0/23	0.0%
31-40	F	0/53	0.0%	0/53	0.0%
	M	0/24	0.0%	0/24	0.0%
41-50	F	0/32	0.0%	0/32	0.0%
	M	0/12	0.0%	0/12	0.0%
51-60	F	0/33	0.0%	0/33	0.0%
	M	0/35	0.0%	0/35	0.0%
61-70	F	0/15	0.0%	0/15	0.0%
	M	0/14	0.0%	0/14	0.0%
71+	F	0/8	0.0%	0/8	0.0%
	M	0/19	0.0%	0/19	0.0%
Total		0/300	0.0%	0/300	0.0%

Samples from Apparently Healthy Blood Donors
BioPlex2200 APLS IgA Prevalence Results by Age and Gender

Age	Gender	aCL IgA		$a\beta_2$GPI IgA	
		Pos/Total	% Prevalence	Pos/Total	% Prevalence
≤20	F	0/14	0.0%	0/14	0.0%
	M	0/5	0.0%	0/5	0.0%
21-30	F	0/13	0.0%	0/13	0.0%
	M	0/23	0.0%	0/23	0.0%
31-40	F	0/53	0.0%	0/53	0.0%
	M	0/24	0.0%	0/24	0.0%
41-50	F	0/32	0.0%	0/32	0.0%
	M	0/12	0.0%	0/12	0.0%
51-60	F	1/33	3.0%	1/33	3.0%
	M	1/35	2.9%	1/35	2.9%
61-70	F	0/15	0.0%	0/15	0.0%
	M	0/14	0.0%	0/14	0.0%
71+	F	0/8	0.0%	0/8	0.0%
	M	0/19	0.0%	0/19	0.0%
Total		2/300	0.7%	2/300	0.7%

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Bio-Rad Laboratories, Inc.
c/o Dr. Juang Wang
Regulatory Affairs Representative
5500 East Second St.
Benicia, CA 94510

MAR 3 0 2012

Re: k103834
Trade/Device Name: BioPlex® 2200 IgG and IgA Kit, Calibrator and Control
Regulation Number: 21 CFR §866.5660
Regulation Name: Multiple autoantibodies immunological test system
Regulatory Class: Class II
Product Code: MID, MSV, JIX, JJX
Dated: March 16, 2012
Received: March 19, 2012

Dear Dr. Wang:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan

Maria M. Chan, Ph.D.
Director
Division Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication(s) for use

510(k) Number (if known): K103834

Device Name: BioPlex® 2200 Antiphospholipid Syndrome IgG and IgA Kits on the BioPlex® 2200 Multi Analyte Detection System
BioPlex® 2200 Antiphospholipid Syndrome IgG and IgA Calibrator Sets
BioPlex® 2200 Antiphospholipid Syndrome IgG and IgA Control Sets

Indications for Use:

The BioPlex® Antiphospholipid Syndrome (APLS) IgG and IgA Kits
The BioPlex® 2200 APLS IgG and IgA kits are multiplex flow immunoassays intended for the semi-quantitative detection of IgG and IgA antibodies to Cardiolipin (CL) and Beta-2 Glycoprotein I (ß2GPI) in human serum and plasma (lithium heparin, sodium heparin, and sodium citrate). In conjunction with other clinical findings, the test systems are used as an aid in the diagnosis of primary Antiphospholipid Syndrome (APS) and those secondary to systemic lupus erythematosus (SLE) or SLE-like disorders.

The BioPlex 2200 APLS IgG and IgA kits are intended for use with the Bio-Rad BioPlex 2200 System

BioPlex® 2200 Antiphospholipid Syndrome (APLS) IgG and IgA Calibrator Sets
The BioPlex® 2200 APLS IgG and IgA Calibrator Sets are intended for the calibration of the corresponding BioPlex® 2200 APLS IgG and IgA Reagent Packs.

BioPlex® 2200 Antiphospholipid Syndrome (APLS) IgG and IgA Control Sets
The BioPlex® 2200 APLS IgG and IgA Control Sets are intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 instrument and the corresponding BioPlex 2200 APLS IgG and IgA Reagent Packs in the clinical laboratory. The performance of the BioPlex 2200 APLS IgG and IgA Control Sets has not been established with any other anti-Cardiolipin and anti- Beta-2 Glycoprotein I IgG or IgA APS assays.

Prescription Use _X_ AND/OR Over-the-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(Please do not write below this line-Continue on another page if needed)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Maria M Chan
Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K103834